REMARKS

Rejection Under 35 USC §112

The Examiner has rejected claims 1-26 on the ground that they are indefinite for failing to particularly point out and distinctly claim the subject matter which is regarded as the invention. Specifically, the Examiner objects to claims 1 and 20 on the ground that they lack a correlation step. Claim 14 has also been rejected on the ground that the preamble recites a method for detecting upper gastrointestinal tract bleeding while the correlation step references lower gastrointestinal tract bleeding.

It is respectfully submitted that these objections have been obviated by amendment.

Rejection Under 35 USC §112, first paragraph

The Examiner has rejected claims 1-26 on the ground that they are allegedly not enabling. Specifically, the Examiner states that the use of a labeled binding partner and an immobilized capture binding partner is critical for the practice of the invention, but is not recited in the claims. Without prejudice, and in order to advance prosecution, independent Claims 1, 8, 14, and 20 have been amended to replace reference to "antiglobin immunointeractive molecule" with "labeled antiglobin immunointeractive molecule". Still further, reference to detection of the globin-antiglobin complex has been clarified to specify that the detection step "comprises immobilization of said globin-antiglobin complex by an immobilized capture molecule". Applicants note that the invention can be designed for use with antibody molecules or, alternatively, some other form of immunointeractive molecule such as a divalent or even a monovalent portion of the Fab region of an antibody. The study of identifying or designing immunointeractive molecules for use in applications such as diagnostics and therapeutics is extremely well developed and the person of skill in the art could, as a matter of routine procedure, select, design or otherwise synthesize an appropriate molecule for use in this invention.

The Examiner has also rejected claims 8-19 on the ground that claims 8 and 14 recite methods for detecting lower and upper gastrointestinal bleeding, but which subject matter is not described in the specification in such a way as to indicate that the applicant had possession of the invention. This rejection is respectfully traversed as the specification clearly provides

support for distinguishing between upper and lower gastrointestinal bleeding. Applicants refer to the following passages as providing examples of this disclosure.

(i) Page 14, lines 15-29: This text describes the movement of a biological sample across a test matrix and the outcomes which can be expected in each region of the test matrix. This text is limited to describing the outcome of the interaction of the heme and/or globin components of any blood in the biological sample with reagents which are impregnated in the test strip. At this point in the text there is no specific description of the differentiation of upper versus lower gastrointestinal tract bleeding.

(ii) Page 18, lines 11-25: This text follows from the text in point (i), above, where a basic description of the mechanical events which occurred during wicking of the biological sample across the test matrix is provided. The text at page 18, however, is directed to describing the interpretation of the results which were obtained. In a first aspect this text describes the fact that the claimed diagnostic test can detect gastrointestinal tract bleeding by analyzing faecal samples for the presence of blood. However, this text goes on to specifically indicate the positive identification of the source of the gastrointestinal tract bleeding, that is differentiation between upper versus lower gastrointestinal tract bleeding. It is indicated that this diagnostic test enables this level of differentiation due to the fact that the heme component of haemoglobin is relatively resistant to breakdown in the small intestine (the upper gastrointestinal tract) while the globin component does not survive passage through the upper gastrointestinal tract. Accordingly,

> *"A positive globin result in a faecal sample therefore indicates that bleeding has occurred in the lower gastrointestinal tract. Accordingly, by applying a combined two-step immunological and non-immunological based test, it is possible to differentiate between upper and lower gastrointestinal tract bleeding wherein a positive heme result together with a negative globin result indicates upper gastrointestinal tract bleeding and a positive heme result together with a positive globin result indicates lower gastrointestinal tract bleeding"*

(iii) Page 29, lines 4-29: This example describes the arrangement of a chromatographic test strip in accordance with the method of the invention. There is provided a figure which

reiterates the design of the test strip is diagrammatic form. The information provided in this example is entirely consistent with that which is described in detail in the description of the invention.

Reconsideration of this rejection is respectfully requested in light of the above.

Rejection Under 35 USC §103

The Examiner has rejected claims 1-26 as lacking inventive step in light of Allison *et al.* (1996) when considered in light of US Patent No. 6,436,721 and International Patent Publication No. WO98/33069. This rejection is respectfully traversed.

Allison *et al.* provides a comparative analysis of three commercially available faecal occult blood tests, these being Hemoccult II, Hemoccult II Sensa and HemeSelect. The authors point out that the latter two tests were developed to provide sensitivity greater than that available using Hemoccult II.

The authors conclude that the use of both Hemoccult II Sensa and HemeSelect to test a stool sample provides a higher level of specificity than the use of any of these tests individually. However, the authors provide no disclosure or discussion in relation to the notion of using an immunological test directed to detecting the globin component of hemoglobin and a chromogen test directed to detecting the heme component of hemoglobin in order to differentiate upper versus lower gastrointestinal tract bleeding. In fact, there is not even any mention of the issue of differentiating upper versus lower gastrointestinal tract bleeding. Consistent with this is the fact that there is no discussion in Allison *et al.* (1996) of the degradation of the globin component of hemoglobin as it passes through the small intestine. Still further, in terms of the Heme Select test, the authors do not indicate whether the antibody which is used binds to the heme component or the globin component of hemoglobin. This is a crucial distinction since an antibody which binds to the heme component of hemoglobin cannot achieve the outcomes of the present invention, being the differentiation of upper versus lower gastrointestinal tract bleeding based, in part, on the detection of the globin component of hemoglobin. It is therefore conceivable that the prior art immunological test may not exclusively detect the globin component, this being a requirement of the present invention.

US 6,436,721 discloses a means for quantifying analytes which are assessed via use of a chromatographic test strip. WO98/33069 discloses an assay device which can be utilized in the context of many different types of immunoassays. Specifically, this latter application describes a device which appears to achieve the absorption and unidirectional flow of an analyte. Both these citations merely disclose means and/or devices for performing improved unidirectional chromatography but provide no further information, which when considered together with Allison *et al.* (1996), would render obvious the notion of differentiating upper versus lower gastrointestinal tract bleeding; nor the notion of how one would design a chromatographic test strip for separately and specifically detecting the heme and globin components of hemoglobin utilizing the combined immunochemical/chromogen based assay. The improvements which are disclosed in these two prior art documents can be applied or used with respect to any test device which requires unidirectional chromatography to occur. However, Applicants' invention lies not with the notion of performing unidirectional chromatography but, rather, with the notion of detecting upper versus lower gastrointestinal tract bleeding based on the unique design of the test strip of the present invention and the combination of analytes which it screens for.

Summary

In light of the above amendment, consideration of the subject patent application is respectfully requested. Any deficiency or overpayment should be charged or credited to Deposit Account No. 500282.

Respectfully submitted,

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